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Patent
Attorney's Docket No. 018413-257

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	
Thomas J. WHALEN *et al.*	Group Art Unit: 1652
Application No.: 09/574,379	Examiner: Shahnam J. Sharareh
Filed: May 19, 2000	
For: NOVEL HIGH VISCOSITY EMBOLIZING COMPOSITIONS	

DECLARATION OF THOMAS J. WHALEN II PURSUANT TO 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

I, THOMAS J. WHALEN II, hereby declare and state:

1. I am a joint inventor for the above-noted application, and am therefore one of the patent Applicants.

2. I received a Bachelor of Science degree from California State University at Long Beach in 1983 and have been employed as a bioengineer for approximately nineteen years. I have been employed by MicroTherapeutics, Inc. ("MTI"), assignee of the entire right, title and interest in this application, for at least the last five years and now have the title of Senior Director of Research and Development.

3. I am a citizen of the United States of America, residing at 958 Capri Road, Encinitas, California 92024.

4. I am a named inventor or named joint inventor on at least six pending United States Patent Applications. In addition, as part of my employment responsibilities for the last five years, I have been the lead investigator for MTI in the evaluation of the effectiveness of both PEC and HVEC compositions (defined below) in *in vivo* animal studies in treating vascular diseases including aneurysms. Furthermore, I have also been the lead investigator for MTI in the clinical evaluations of HVECs in treating aneurysms in human subjects. As part of my responsibilities, I have observed well over fifty clinical procedures involving the treatment of aneurysms using HVECs.

5. I have reviewed the above-noted application, United States Patent Application Serial Number 09/574,379 ("the '379 application"), entitled "Novel High Viscosity Embolizing Compositions," including the Office Action mailed on December 3, 2001, and the publications cited therein. I have also reviewed the Declaration of Dr. Richard J. Greff dated August 30, 2001, which was submitted to the Patent Office on September 10, 2001.[1]

[1] Dr. Greff's Declaration sets forth corrections to the concentrations of ingredients contained in Examples 2 and 4 of the '379 application.

6. The subject matter described in the '379 application relates to compositions which may be used to treat aneurysms. The '379 application provides background information on the treatment of aneurysms and explains that embolic compositions prior to our invention comprised a biocompatible polymer, a biocompatible solvent, and a contrast agent. Embolic compositions prior to our invention, or "Preceding Embolic Compositions" ("PECs") have a low concentration of polymer (e.g., less than eight weight percent, based on the total weight of the composition). The compositions used in the treatment of aneurysms in animal studies prior to our invention had a low viscosity (e.g., about 90 centiStokes or less at 40°C).

7. Although the PECs had many benefits and were useful in treating many patients, I observed certain drawbacks associated with using the PECs in the treatment of aneurysms. Specifically, upon ejection of the PECs into an aneurysmal sac, an elongated, string-like mass forms *in vivo* often at a distance from the catheter tip. This mass is sufficiently mobile that a flow-arresting balloon was required to inhibit unwanted migration of the formed mass from the aneurysmal sac into the vasculature. With the use of a flow-arresting balloon, the formed mass was less mobile but was observed to be of sufficient mobility to migrate from the aneurysmal sac into the vasculature which can lead to ischemia, stroke and/or hemorrhage in the treated animal.

8. This undesired migration was confirmed by my observations that ejection of the PECs *in vivo* resulted in embolization not at the target site, but at arteries attendant to the target site. In addition, the masses formed upon ejection of the PECs were prone to fragmentation. Such fragmentation sometimes led to the incapacitation or death of the animal.

9. Contrarily, I have observed that the use of High Viscosity Embolic Compositions ("HVECs"), as described in the '379 application, represent a significant advance in the art. Specifically, HVECs are more effective in treating aneurysms because they significantly reduce the side-effects of the low viscosity PECs as I described above. In animal studies evaluating the use of PECs in treating aneurysms, an unacceptable level of migration and/or fragmentation occurred which rendered inappropriate the use of PECs clinically. On the other hand, in animal studies evaluating the use of HVECs in treating aneurysms, no migration and/or fragmentation was observed, which was confirmed by *in vitro* filtration tests and by *in vivo* high-definition X-ray analysis. In view of the above, HVECs were allowed for use in clinical evaluations.

10. In my opinion, the above results obtained using these HVECs are surprising and unexpected. First, it could not have been predicted that HVECs would be less prone to fragmentation *in vivo* as compared to PECs. This reduction in fragmentation is critical to the effectiveness of HVECs in treating aneurysms. Secondly, it also could not have been predicted that HVECs would form a solid mass of significantly reduced migration or that the mass would not be displaced from the aneurysmal sac. That is to say that simply having a mass with reduced migration is insufficient if the mass migrates out of the aneurysmal sac (see the note above regarding PECs and the use of a flow arresting balloon).

11. These unexpected results were further demonstrated by dissection of animals treated in an aneurysmal sac with PECs. All of the animals treated had a majority of the mass formed *in vivo* at a point in the vasculature significantly downstream of the ejection site with or without the use of a flow arresting balloon. This evidenced significant migration of the formed mass out of the aneursymal sac. Contrarily, animals treated in the aneursysmal sac with HVECs had the majority, if not all, of the mass formed *in vivo* retained in the sac.

12. I declare further than all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the '379 application or any patent issuing thereon.

3/14/02
Date

Thomas J. Whalen II